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SUBJECT: SAR Analysis of a Benzoxazine Inert Ingredient

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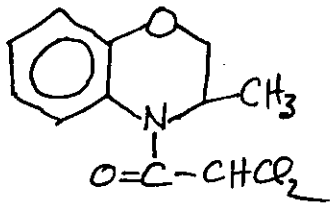
I performed an SAR analysis of the benzoxazine shown below: 4-(dichloroacetyl)-3,4-dihydro-3-methyl-2H-1,4-benzoxazine.



A tolerance has been requested for this chemical when used as an inert ingredient in a formulation containing metolachlor, for which tolerances have been established.

Toxicity endpoints were considered as follows:

oncogenicity
mutagenicity
teratogenicity
neurotoxicity.

The techniques utilized included the following:

1. Methods used by the OTS SAT for predicting absorption through the several routes.

2. Examination for activating substructures for carcinogenicity and mutagenicity.

3. Comparison with molecules active as developmental toxicants or neurotoxicants.

A phone consultation was also conducted with Yin-Tac Woo, member of the SAT and the HED Peer Review Committee.

Conclusion:
There is a definite nitrosamine concern for the deacetylated

molecule. I understand from the Inerts PM (Kerry Leifer) that nitrosamines are undetectable in this formulation. None of the other endpoints listed above showed an obvious trigger with this molecule. The statement of Dr. Woo is that he would consider the molecule of low-moderate concern for oncgenicity. He did not mention the nitrosamine concern, which occurred to me after talking with him.

This set of data requirements was intended to provide information on the effects of the inert ingredient on human health and the environment, and would allow the Agency to determine the conditions of safe use of inert ingredients in pesticide formulations.

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Residue chemistry data requirements involve a description of the types and use patterns of pesticides in which the inert ingredient will be used. Product chemistry data requirements include structural information and physical/chemical characteristics. The toxicology data requirements include mutagenicity studies, developmental effects studies, and subchronic toxicity studies. The ecotoxicology requirements include a battery of four acute aquatic and avian toxicity studies. Environmental fate data requirements include hydrolysis, aquatic photolysis, soil photolysis, aerobic soil metabolism, and leaching and adsorption/desorption studies.

The inert ingredient data requirements listed in Part 158.1000 comprise the "base set" of data which will be required for the majority of inert ingredients. In some cases, additional studies on inert ingredients may be required. Additional data requirements beyond the minimum requirements will be determined by a tiered approach which will be based upon the results of the "base set studies. For example, depending upon the results of the toxicology studies and the use pattern of pesticide products containing a given inert ingredient, actual residue data and/or chronic toxicity studies may be required.

"Inert ingredient" means any substance (or group of structurally similar substances if designated by the Agency), other than an active ingredient, which is intentionally included in a pesticide product.

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